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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6	Mar 08	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
NEWS 11	Apr 02	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS 12	Apr 08	"Ask CAS" for self-help around the clock
NEWS 13	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 14	Apr 09	ZDB will be removed from STN
NEWS 15	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 18	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 19	Jun 03	New e-mail delivery for search results now available
NEWS 20	Jun 10	MEDLINE Reload
NEWS 21	Jun 10	PCTFULL has been reloaded
NEWS 22	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 23	Jul 19	NTIS to be reloaded July 28, 2002

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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=> HCV and envelope
          5531 HCV
            14 HCVS
          5534 HCV
                 (HCV OR HCVS)
         41663 ENVELOPE
          7861 ENVELOPES
         46283 ENVELOPE
                 (ENVELOPE OR ENVELOPES)
L1         456 HCV AND ENVELOPE

=> E1 or E2 and L1
'E1' NOT FOUND
The E# entered is not currently defined.

=> E1 and L1
'E1' NOT FOUND
The E# entered is not currently defined.

=> envelope 1 and L1
         41663 ENVELOPE
          7861 ENVELOPES
```

```
         46283 ENVELOPE
                 (ENVELOPE OR ENVELOPES)
       7186860 1
            60 ENVELOPE 1
                 (ENVELOPE(W)1)
L2           21 ENVELOPE 1 AND L1

=> D L2 IBIB TI SO AU ABS 1-21

L2   ANSWER 1 OF 21  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2002:224906  CAPLUS
DOCUMENT NUMBER:         136:339231
TITLE:                   Early changes in hepatitis C viral quasispecies
during
                         interferon therapy predict the therapeutic outcome
AUTHOR(S):               Farci, Patrizia; Strazzera, Rita; Alter, Harvey J.;
                         Farci, Stefania; Degioannis, Daniela; Coiana,
                         Alessandra; Peddis, Giovanna; Usai, Francesco; Serra,
                         Giancarlo; Chessa, Luchino; Diaz, Giacomo;
                         Balestrieri, Angelo; Purcell, Robert H.
CORPORATE SOURCE:        Department of Medical Sciences, University of
                         Cagliari, Cagliari, 09124, Italy
SOURCE:                  Proceedings of the National Academy of Sciences of
the
                         United States of America (2002), 99(5), 3081-3086
                         CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:               National Academy of Sciences
DOCUMENT TYPE:           Journal
LANGUAGE:                English
TI   Early changes in hepatitis C viral quasispecies during interferon therapy
     predict the therapeutic outcome
SO   Proceedings of the National Academy of Sciences of the United States of
     America (2002), 99(5), 3081-3086
     CODEN: PNASA6; ISSN: 0027-8424
AU   Farci, Patrizia; Strazzera, Rita; Alter, Harvey J.; Farci, Stefania;
     Degioannis, Daniela; Coiana, Alessandra; Peddis, Giovanna; Usai,
     Francesco; Serra, Giancarlo; Chessa, Luchino; Diaz, Giacomo; Balestrieri,
     Angelo; Purcell, Robert H.
AB   Despite recent treatment advances, the majority of patients with chronic
     hepatitis C fail to respond to antiviral therapy.  Although the genetic
     basis for this resistance is unknown, accumulated evidence suggests that
     changes in the heterogeneous viral population (quasispecies) may be an
     important determinant of viral persistence and response to therapy.
     Sequences within hepatitis C virus (HCV) envelope
     1 and envelope 2 genes, inclusive of the hypervariable
     region 1, were analyzed in parallel with the level of viral replication
in
     serial serum samples obtained from 23 patients who exhibited different
     patterns of response to therapy and from untreated controls.  Our study
     provides evidence that although the viral diversity before treatment does
     not predict the response to treatment, the early emergence and dominance
     of a single viral variant distinguishes patients who will have a
sustained
     therapeutic response from those who subsequently will experience a
     breakthrough or relapse.  A dramatic redn. in genetic diversity leading
to
     an increasingly homogeneous viral population was a consistent feature
     assocd. with viral clearance in sustained responders and was independent
     of HCV genotype.  The persistence of variants present before
     treatment in patients who fail to respond or who experience a
breakthrough
```

during therapy strongly suggests the preexistence of viral strains with inherent resistance to IFN. Thus, the study of the evolution of the **HCV** quasispecies provides prognostic information as early as the first 2 wk after starting therapy and opens perspectives for elucidating the mechanisms of treatment failure in chronic hepatitis C.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:912910 CAPLUS
TITLE: Secretory expression of different C-terminal truncated **HCV** E1 proteins in mammalian cells and characterization of the expressed products
AUTHOR(S): Zhu, Jun; Kong, Yuying; Liu, Jing; Zhang, Zuchuan; Wang, Yuan; Li, Guangdi
CORPORATE SOURCE: Institute of Biochemistry and Cell Biology, Shanghai Institute for Biological Sciences, Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China
SOURCE: Shengwu Huaxue Yu Shengwu Wuli Xuebao (2001), 33(6), 634-640
CODEN: SHWPAU; ISSN: 0582-9879
PUBLISHER: Shanghai Kexue Jishu Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

TI Secretory expression of different C-terminal truncated **HCV** E1 proteins in mammalian cells and characterization of the expressed products

SO Shengwu Huaxue Yu Shengwu Wuli Xuebao (2001), 33(6), 634-640
CODEN: SHWPAU; ISSN: 0582-9879

AU Zhu, Jun; Kong, Yuying; Liu, Jing; Zhang, Zuchuan; Wang, Yuan; Li, Guangdi

AB Three fragments of **HCV envelope 1** (E1) with different C- terminal truncation at aa310, aa325, aa340 were cloned into the mammalian expression vector pSecTagB. An epitope in the hepatitis B surface antigen, preS1(21-47), were genetically engineered onto the N-terminus of the recombinant protein and used as an affinity tag for detection and purifn. The resulting pSec-preS1-E1t310, pSec-preS1-E1t325, and pSec- preS1-E1t340 were transiently expressed in the HeLa cells and antigenicity, secretory efficiency, and glycosylation type of the recombinant E1 proteins were compared. All of the three recombinant proteins could be detected by both preS1 monoclonal antibody and E1 polyclonal antiserum. The expression products were secreted and highly mannose-type glycosylated, with S1E1t325 being secreted, indicating the influence of the hydrophobic regions on the secretion of the E1 protein. Three CHO cell lines expressing the proteins, S1E1t310, S1E1t325, and S1E1t340, were established and CHO/pSecS1E1t325 was chosen for further study. The secreted S1E1t325 could be enriched from cell culture medium by the preS1 antibody-coupled Sepharose. The glycosylation anal. indicated the lack of complex glycogen even after the E1 was secreted via Golgi complexes. The established stable cell lines and anti-preS1 affinity method could be utilized to enrich and purify the **HCV** E1 expressed in mammalian cells, and may be used for further characterization of this protein.

L2 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:888331 CAPLUS

DOCUMENT NUMBER: 136:133500
TITLE: Hepatitis C virus core and **envelope** proteins do not suppress the host's ability to clear a hepatic viral infection
AUTHOR(S): Sun, Jiaren; Bodola, Francis; Fan, Xuegong; Irshad, Habib; Soong, Lynn; Lemon, Stanley M.; Chan, Teh-Sheng
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Texas Medical Branch at Galveston, Galveston, TX, 77555-1070, USA
SOURCE: Journal of Virology (2001), 75(24), 11992-11998
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

TI Hepatitis C virus core and **envelope** proteins do not suppress the host's ability to clear a hepatic viral infection

SO Journal of Virology (2001), 75(24), 11992-11998
CODEN: JOVIAM; ISSN: 0022-538X

AU Sun, Jiaren; Bodola, Francis; Fan, Xuegong; Irshad, Habib; Soong, Lynn; Lemon, Stanley M.; Chan, Teh-Sheng

AB Several hepatitis C virus (**HCV**) proteins have been shown in vitro to interact with host cellular components that are involved in immune regulation. However, there is a paucity of data supporting the relevance of these observations to the in vivo situation. To test the hypothesis that such an interaction suppresses immune responses, the authors studied a line of transgenic C57BL/6 mice that express the **HCV** core and **envelope** proteins in the liver. The potential effects of these proteins on the hepatic immune response were evaluated by challenging these mice with a hepatotropic adenovirus. Both transgenic and nontransgenic mice developed similar courses of infection and cleared the virus from the liver by 28 days post-infection. Both groups of mice mounted similar IgG, IgG2a, interleukin-2, and tumor necrosis factor alpha responses against the virus. Addnl., BALB/c mice were able to clear infection with recombinant adenovirus that does or does not express the **HCV** core and **envelope 1** proteins in the same manner. These data suggest that **HCV** core and **envelope** proteins do not inhibit the hepatic antiviral mechanisms in these murine exptl. systems and thus favor a model in which **HCV** circumvents host responses through a mechanism that does not involve general suppression of intrahepatic immune responses.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:445658 CAPLUS
DOCUMENT NUMBER: 136:178463
TITLE: Investigating hepatitis C virus heterogeneity in a high prevalence setting using heteroduplex tracking analysis
AUTHOR(S): Sullivan, D. G.; Kim, S. S.; Wilson, J. J.; Stehman-Breen, C.; Gretch, D. R.
CORPORATE SOURCE: Department of Laboratory Medicine, University of Washington Medical Center, Seattle, WA, 98104-2499, USA
SOURCE: Journal of Virological Methods (2001), 96(1), 5-16
CODEN: JVMEDH; ISSN: 0166-0934

PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Investigating hepatitis C virus heterogeneity in a high prevalence setting
using heteroduplex tracking analysis
SO Journal of Virological Methods (2001), 96(1), 5-16
CODEN: JVMEDH; ISSN: 0166-0934
AU Sullivan, D. G.; Kim, S. S.; Wilson, J. J.; Stehman-Breen, C.; Gretch, D. R.
AB Hepatitis C virus (**HCV**) infection is very common among chronic hemodialysis patients. In the past, blood transfusion appeared to be the primary risk factor; however evidence of nosocomial **HCV** transmission in the hemodialysis setting has recently been reported. This report describes a mol. investigation of **HCV** isolates obtained from a population of 670 patients attending six different Seattle-King County based hemodialysis centers in order to identify potential common source infections. Seven hundred thirty-three serum specimens were collected from hemodialysis patients in 1992 and 1996, and were tested for **HCV** antibodies and RNA. Overall, 115 of 670 (17%) patients were pos. for **HCV** RNA, and thus were considered actively infected by **HCV**. **HCV** genotype was detd. in all cases by restriction fragment length polymorphism, and 93 patients were found to be infected by **HCV** genotype 1. **HCV envelope** genes were amplified from the 93 patients with genotype 1 infection, and were studied in further detail by heteroduplex tracking anal. (HTA) using genotype 1a and 1b specific probes derived from the **envelope 1** (E1) and **envelope** 2 (E2) genes. Genetic relatedness between pairs of **HCV envelope** genes was estd. by calcg. the degree of gel shift relative to homoduplex controls. Nucleotide sequencing and phylogenetic anal. was used to confirm genetic relatedness detected by HTA. When HTA was performed using the E1 gene probe, 12 apparently related infections were detected; 10 of 12 (83%) of these infections were confirmed as truly related using the gold std. method of nucleotide sequencing plus phylogenetic anal. Using an E2 gene probe, 24 infections were apparently related, but only six (25%) were confirmed by sequencing. As a control, 41 **envelope** genes, which were unrelated by HTA, were sequenced; 0 of 41 (0%) were truly related. In summary, HTA provides a rapid and effective mol. technique for screening **HCV** genetic relatedness in population-based studies, and should prove valuable in future studies of **HCV** mol. epidemiol.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:328609 CAPLUS
DOCUMENT NUMBER: 135:353459
TITLE: Prokaryotic expression of hepatitis C virus **envelope 1** gene and application of expressed product
AUTHOR(S): Gao, Jian'en; Tao, Qimin; Ma, Dalong; Feng, Baifang; Ji, Heping; Ji, Ying
CORPORATE SOURCE: Hepatology Institute of Beijing Medical University, People's Hospital, Beijing, 100044, Peop. Rep. China

SOURCE: Zhonghua Shiyan He Linchuang Bingduxue Zazhi (2001), 15(1), 20-23
CODEN: ZSLZFS; ISSN: 1003-9279
PUBLISHER: Zhonghua Shiyan He Linchuang Bingduxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

TI Prokaryotic expression of hepatitis C virus **envelope 1** gene and application of expressed product

SO Zhonghua Shiyan He Linchuang Bingduxue Zazhi (2001), 15(1), 20-23
CODEN: ZSLZFS; ISSN: 1003-9279

AU Gao, Jian'en; Tao, Qimin; Ma, Dalong; Feng, Baifang; Ji, Heping; Ji, Ying

AB The **HCV** E1 gene was expressed in E. coli. The expression vector was constructed by ligation of **HCV** E1 sequence, which was amplified by RT-PCR methods from 50 .mu.l of **HCV** RNA pos. serum using primers specific to the **HCV** E1 sequence, to the prokaryotic expression vector PMS-31b transfected POP2136 at 16.degree. for 16 h. The recombinant plasmid was screened out and characterized by restriction enzyme anal. The bacteria contg. the recombinant plasmid was induced at 42.degree. for 4 h, and the recombinant protein was visualized by SDS-PAGE. The specificity of the recombinant protein was detd. by Western blot assay. After purifn. of the expressed protein, this protein was coated on the plate with the concn. of 2 .mu.g/mL in pH 9.6 buffer at 4.degree. for overnight, and the serum specimen was tested at the diln. of 1:20 by ELISA. Two fragments could be seen on the SDS-PAGE after digestion of the RT-PCR product with SmaI. And there emerged one fragment of 356 bp after digesting the recombinant plasmid with SmaI and XbaI. A band of 30,000 could be seen on the SDS-PAGE after the induction of bacteria contg. the recombinant plasmid pMS-E1 at 42.degree. for 4 h. The ELISA result indicated that 28.9% (26/90) anti-**HCV** pos. serum were anti-**HCV** E1 pos., but 3.9%(3/76) were pos. in the anti-**HCV** neg. serum. The **HCV** E1 sequence from **HCV** RNA pos. serum has been expressed in E. coli. The expression rate is about 17% of the total protein of the bacteria. This protein possessed good specificity and may be used in the diagnosis of **HCV** infection.

L2 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:212987 CAPLUS
DOCUMENT NUMBER: 136:1134
TITLE: Genome of human hepatitis C virus (**HCV**): Gene organization, sequence diversity, and variation
AUTHOR(S): Kato, Nobuyuki
CORPORATE SOURCE: Department of Molecular Biology, Institute of Cellular and Molecular Biology, Okayama University Medical School, Okayama, 700-8558, Japan
SOURCE: Microbial & Comparative Genomics (2000), 5(3), 129-151
CODEN: MCGEFP; ISSN: 1090-6592
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

TI Genome of human hepatitis C virus (**HCV**): Gene organization, sequence diversity, and variation

SO Microbial & Comparative Genomics (2000), 5(3), 129-151
CODEN: MCGEFP; ISSN: 1090-6592

AU Kato, Nobuyuki

AB A review with refs. Hepatitis C virus (**HCV**) is the major etiol. agent of non-A, non-B hepatitis. **HCV** infection frequently causes chronic hepatitis, which progresses to liver cirrhosis and hepatocellular carcinoma. Since the discovery of **HCV** in 1989, a large no. of genetic analyses of **HCV** have been reported, and the viral genome structure has been elucidated. An enveloped virus, **HCV** belongs to the family Flaviviridae, whose genome consists of a pos.-stranded RNA mol. of about 9.6 kilobases and encodes a large polyprotein precursor (about 3000 amino acids). This precursor protein is cleaved by the host and viral proteinase to generate at least 10 proteins: the core, **envelope 1** (E1), E2, p7, nonstructural (NS) 2, NS3, NS4A, NS4B, NS5A, and NS5B. These **HCV** proteins not only function in viral replication but also affect a variety of cellular functions. **HCV** has been found to have remarkable genetic heterogeneity. To date, more than 30 **HCV** genotypes have been identified worldwide. Furthermore, **HCV** may show quasispecies distribution in an infected individual. These findings may have important implications in diagnosis, pathogenesis, treatment, and vaccine development. The hypervariable region 1 found within the **envelope** E2 protein was shown to be a major site for the genetic evolution of **HCV** after the onset of hepatitis, and might be involved in escape from the host immunesurveillance system.

REFERENCE COUNT: 241 THERE ARE 241 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:892533 CAPLUS
DOCUMENT NUMBER: 135:57401
TITLE: Expression and membrane association of hepatitis C virus **envelope 1** protein
AUTHOR(S): Ciccaglione, Anna Rita; Marcantonio, Cinzia; Costantino, Angela; Equestre, Michele; Geraci, Andrea; Rapicetta, Maria
CORPORATE SOURCE: Laboratory of Virology, Istituto Superiore di Sanita, Rome, 00161, Italy
SOURCE: Virus Genes (2000), 21(3), 223-226
CODEN: VIGEET; ISSN: 0920-8569
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

TI Expression and membrane association of hepatitis C virus **envelope 1** protein
SO Virus Genes (2000), 21(3), 223-226
CODEN: VIGEET; ISSN: 0920-8569
AU Ciccaglione, Anna Rita; Marcantonio, Cinzia; Costantino, Angela; Equestre, Michele; Geraci, Andrea; Rapicetta, Maria
AB The expression of hepatitis C virus (**HCV**) E1 protein is toxic for Escherichia coli cells. For this reason, we have cloned the E1 gene in the pET3a vector and analyzed the inducible expression of the protein in two strains of E. coli characterized by a different level of redn. of basal synthesis. The results indicated that synthesis of E1 was supported only by the BL21(DE3)pLysS strain which provides a tightest control of protein expression before the induction. The BL21(DE3)pLysS cells were

then used for the expression of E1 gene, varying at its carboxy terminus in order to retain (E1, aa 192-383) or delete (E1t, aa 192-340) a C-terminal hydrophobic region that may be involved in membrane assocn. Following cell fractionation, E1 protein was found assocd. with the membrane fraction. By contrast, the truncated mutant E1t, was identified in the sol. phase suggesting a direct role for the C-terminal domain in E1
membrane assocn.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:419879 CAPLUS
DOCUMENT NUMBER: 133:307447
TITLE: A novel hepatitis C virus (**HCV**) subtype from Somalia and its classification into **HCV** clade 3
AUTHOR(S): Abid, Karim; Quadri, Rafael; Veuthey, Anne-Lise; Hadengue, Antoine; Negro, Francesco
CORPORATE SOURCE: Division of Gastroenterology and Hepatology, University Hospital, Geneva, 1211, Switz.
SOURCE: Journal of General Virology (2000), 81(6), 1485-1493
CODEN: JGVIAY; ISSN: 0022-1317
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
TI A novel hepatitis C virus (**HCV**) subtype from Somalia and its classification into **HCV** clade 3
SO Journal of General Virology (2000), 81(6), 1485-1493
CODEN: JGVIAY; ISSN: 0022-1317
AU Abid, Karim; Quadri, Rafael; Veuthey, Anne-Lise; Hadengue, Antoine; Negro, Francesco
AB Hepatitis C virus (**HCV**) sequences from throughout the world have been grouped into six clades, based on recently proposed criteria. Here, the partial sequences and clade assignment are reported for three **HCV** isolates from chronic hepatitis C patients from Somalia, for whom conventional assays failed to identify the genotype. Phylogenetic anal. of the sequences of the core, **envelope 1** and part of the non-structural 5b regions suggests that all three isolates belong to a distinct **HCV** genetic group, tentatively classified as subtype 3h. This novel **HCV** subtype shows the highest sequence similarity with **HCV** isolates from Indonesia. Despite the fact that these patients were infected with **HCV** clade 3, none of them responded to std. interferon treatment.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:413510 CAPLUS
DOCUMENT NUMBER: 131:209940
TITLE: Why is the interferon sensitivity-determining region (ISDR) system useful in Japan?
AUTHOR(S): Nakano, Isao; Fukuda, Yoshihide; Katano, Yoshiaki; Nakano, Satoshi; Kumada, Takashi; Hayakawa, Tetsuo
CORPORATE SOURCE: Second Department of Internal Medicine, Nagoya

University School of Medicine, Nagoya, 466-8550, Japan
SOURCE: Journal of Hepatology (1999), 30(6), 1014-1022
CODEN: JOHEEC; ISSN: 0168-8278
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Why is the interferon sensitivity-determining region (ISDR) system useful in Japan?
SO Journal of Hepatology (1999), 30(6), 1014-1022
CODEN: JOHEEC; ISSN: 0168-8278
AU Nakano, Isao; Fukuda, Yoshihide; Katano, Yoshiaki; Nakano, Satoshi; Kumada, Takashi; Hayakawa, Tetsuo
AB The amino acid sequence of NS5A2209-2248, named the "interferon sensitivity-detg. region" (ISDR), has been reported to correlate with responsiveness of interferon (IFN) therapy to patients with the hepatitis C virus (**HCV**) genotype-1b, by several Japanese authors. However, European authors have failed to find this phenomenon, suggesting a difference in **HCV**-1b isolates between Japan and Europe. We compared the **HCV**-1b nucleotide sequences of our Japanese patients and those of other countries quoted from GenBank, using the **envelope 1** sequence. A phylogenetic tree anal. revealed two characteristic groups from a geog. viewpoint: one group (NJ group) consists of almost entirely non-Japanese isolates, and the other (J group) of almost entirely Japanese isolates. The isolates other than the NJ and J groups are characterized by their specific nucleotide residue, constructing an individual group (W group). Japanese **HCV**-1b isolates consist of the J group and W group (approx. 40% and 60%, resp.). Comparative study between the two groups in Japanese patients treated with IFN revealed a strong correlation between ISDR type and IFN responsiveness only in the J group, but not in the W group. These observations convinced us that the existence of the Japan-specific J group is one reason why the ISDR system is useful only in Japan.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:67576 CAPLUS
DOCUMENT NUMBER: 126:129053
TITLE: Classification of hepatitis C virus variants in six major types based on analysis of the **envelope 1** and nonstructural 5B genome regions and complete polyprotein sequences
AUTHOR(S): de Lamballerie Xavier; Charrel, Remi N.; Attoui, Houssam; De Micco, Philippe
CORPORATE SOURCE: Faculte Medecine, Hopital Timone, Marseille, 13385, Fr.
SOURCE: Journal of General Virology (1997), 78(1), 45-51
CODEN: JGVIAY; ISSN: 0022-1317
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Classification of hepatitis C virus variants in six major types based on analysis of the **envelope 1** and nonstructural 5B genome

regions and complete polyprotein sequences
SO Journal of General Virology (1997), 78(1), 45-51
CODEN: JGVIAY; ISSN: 0022-1317
AU de Lamballerie Xavier; Charrel, Remi N.; Attoui, Houssam; De Micco, Philippe
AB The phylogenetic status of recently described isolates of hepatitis C virus (**HCV**) from Vietnam, Thailand and Indonesia (previously classified as types 7, 8, 9, 10 and 11) was re-analyzed by the neighbor-joining method instead of the unweighted pair-group method with arithmetic mean (UPGMA) that was first used by the discoverers of these strains. The anal. of complete amino acid sequences and of nucleotide sequences of the **envelope 1** (672 nt) and nonstructural 5B (1092 nt) genomic regions permitted the re-assignment of the type 7, 8, 9 and 11 isolates to type 6, and that of type 10 strains to type 3. Finally, this study made possible the classification of the previously described **HCV** strains (including these South-East Asian isolates) in six major types and at least 30 subtypes. It confirms that anal. of the E1 and NS5B genomic regions using the neighbor-joining method is a reliable tool for the assignment of most new isolates.

L2 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:637827 CAPLUS
DOCUMENT NUMBER: 125:325919
TITLE: Treatment with recombinant interferon-.alpha.2a for patients with chronic hepatitis C: predictive factors for biochemical and virologic response
AUTHOR(S): Hagiware, H.; Hayashi, N.; Kasahara, A.; Oshita, M.; Katayama, K.; Kato, M.; Masuzawa, M.; Fusamoto, H.; Sakurai, M.; et al.
CORPORATE SOURCE: First Dept. Med., Osaka Univ. School of Medicine, Osaka, Japan
SOURCE: Scand. J. Gastroenterol. (1996), 31(10), 1021-1026
CODEN: SJGRA4; ISSN: 0036-5521
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Treatment with recombinant interferon-.alpha.2a for patients with chronic hepatitis C: predictive factors for biochemical and virologic response
SO Scand. J. Gastroenterol. (1996), 31(10), 1021-1026
CODEN: SJGRA4; ISSN: 0036-5521
AU Hagiware, H.; Hayashi, N.; Kasahara, A.; Oshita, M.; Katayama, K.; Kato, M.; Masuzawa, M.; Fusamoto, H.; Sakurai, M.; et al.
AB The heterogeneity of the hepatitis C virus (**HCV**) genome has been reported to be assocd. with the effectiveness of interferon therapy. We investigated the correlation of the viral and host factors, including the degree of sequence complexity of the **HCV** genome for responses to interferon-.alpha. in patients with chronic hepatitis C. Ninety-seven patients received a 26-wk course of recombinant interferon-.alpha.2a therapy. The sequence complexity of the **envelope 1**-2 region was evaluated by polymerase chain reaction-mediated single-strand conformation polymorphism (PCR-SSCP) anal. Of the 85 patients who completed the treatment, 31 (36%) achieved a sustained response, and 28 (33%) showed a sustained loss of **HCV** RNA. A low **HCV** RNA level, detd. by the branched DNA probe assay, and serotype group 2 **HCV** correlated with a sustained response. In patients with serotype group 1 **HCV** of more than the threshold of the branched DNA probe assay, a band no. on PCR-SSCP anal. of more than 2 could be assocd. with inefficacy of interferon therapy. Multivariate anal. in the 50 patients whose sera were available for all the virol. tests showed that

only the **HCV** RNA level is independently predictive of a sustained response. Detn. of the **HCV** RNA level is most important for predicting the response before interferon therapy.
PCR-SSCP
anal. may be useful as an addnl. test for patients with a high **HCV** RNA level of serotype group 1 **HCV**.

L2 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:336531 CAPLUS
DOCUMENT NUMBER: 125:5386
TITLE: Nucleotide and amino acid sequences of the **envelope 1** and core genes of hepatitis C virus isolates
INVENTOR(S): Bukh, Jens; Miller, Roger H.; Purcell, Robert H.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 338 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9605315	A2	19960222	WO 1995-US10398	19950815
WO 9605315	A3	19960404		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5882852	A	19990316	US 1994-290665	19940815
AU 9534065	A1	19960307	AU 1995-34065	19950815
AU 712385	B2	19991104		
EP 779924	A2	19970625	EP 1995-930831	19950815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.:
US 1994-290665 A 19940815
US 1993-86428 A2 19930629
WO 1995-US10398 W 19950815

TI Nucleotide and amino acid sequences of the **envelope 1** and core genes of hepatitis C virus isolates
SO PCT Int. Appl., 338 pp.
CODEN: PIXXD2
IN Bukh, Jens; Miller, Roger H.; Purcell, Robert H.
AB The nucleotide and deduced amino acid sequences of cDNAs encoding the **envelope** (**1**) genes and core genes of isolates of hepatitis C virus (**HCV**) are disclosed. Information derived from these sequences is useful in classification of viral isolates and in the development of immunochem. and nucleic acid reagents for detection of the virus and in vaccines.

L2 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:295079 CAPLUS
DOCUMENT NUMBER: 124:352673
TITLE: Recombinant production and purification of hepatitis C
virus **envelope** proteins for diagnostic and

therapeutic use
INVENTOR(S): Maertens, Geert; Bosman, Fons; De Martynoff, Guy; Buyse, Marie-Ange
PATENT ASSIGNEE(S): Innogenetics N.V., Belg.
SOURCE: PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9604385	A2	19960215	WO 1995-EP3031	19950731
WO 9604385	A3	19960307		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2172273	AA	19960215	CA 1995-2172273	19950731
AU 9533824	A1	19960304	AU 1995-33824	19950731
AU 708174	B2	19990729		
EP 721505	A1	19960717	EP 1995-930434	19950731
EP 721505	B1	20020508		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09503396	T2	19970408	JP 1995-506189	19950731
BR 9506059	A	19971028	BR 1995-6059	19950731
AT 217345	E	20020515	AT 1995-930434	19950731
EP 1211315	A1	20020605	EP 2002-3643	19950731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 6150134	A	20001121	US 1996-612973	19960311
US 6245503	B1	20010612	US 1997-927597	19970911

PRIORITY APPLN. INFO.:
EP 1994-870132 A 19940729
EP 1995-930434 A3 19950731
WO 1995-EP3031 W 19950731
US 1996-612973 A3 19960311

TI Recombinant production and purification of hepatitis C virus **envelope** proteins for diagnostic and therapeutic use

SO PCT Int. Appl., 146 pp.
CODEN: PIXXD2

IN Maertens, Geert; Bosman, Fons; De Martynoff, Guy; Buyse, Marie-Ange

AB **Envelope** proteins E1 and E2 of hepatitis C virus (**HCV**), their recombinant prodn. and purifn., their fragments and engineered derivs., their antigenic epitope peptides, their monoclonal antibodies, and their use for diagnostic and therapeutic means are provided. A method is described for purifying recombinant **HCV** single or specific oligomeric **envelope** proteins, characterized in that upon lysing the transformed host cells to isolate the recombinantly expressed protein a disulfide bond cleavage or redn. step is carried out with a disulfide bond cleavage agent (such as dithiothreitol and/or Empigen BB) and an SH group protecting agent (such as N-ethylmaleimide). Various forms of the E1 and E2 proteins are constructed by std. genetic techniques using vaccinia virus recombination vectors; such proteins are specific for various **HCV** genotypes, may delete the hydrophobic region from

E1, or remove various glycosylation sites; they may also add factor Xa cleavage sites and His6 tags for improved purifn. Epitope (such as F, G, H, and I) peptides are used to generate monoclonal antibodies and to monitor disease progression in patients. Furthermore, the **HCV** E1 protein and peptides are used for prognosing and monitoring the clin. effectiveness and/or clin. outcome of **HCV** treatment.

L2 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:872888 CAPLUS
DOCUMENT NUMBER: 123:307536
TITLE: In vivo transfection of hepatitis C virus complementary DNA into rodent liver by asialoglycoprotein receptor mediated gene delivery
AUTHOR(S): Yamamoto, Masato; Hayashi, Norio; Miyamoto, Yasuhide; Takehara, Tetsuo; Mita, Eiji; Seki, Makoto; Fusamoto, Hideyuki; Kamada, Takenobu
CORPORATE SOURCE: School Medicine, Osaka University, Osaka, 565, Japan
SOURCE: Hepatology (Philadelphia) (1995), 22(3), 847-55
CODEN: HPTLD9; ISSN: 0270-9139
DOCUMENT TYPE: Journal
LANGUAGE: English
TI In vivo transfection of hepatitis C virus complementary DNA into rodent liver by asialoglycoprotein receptor mediated gene delivery
SO Hepatology (Philadelphia) (1995), 22(3), 847-55
CODEN: HPTLD9; ISSN: 0270-9139
AU Yamamoto, Masato; Hayashi, Norio; Miyamoto, Yasuhide; Takehara, Tetsuo; Mita, Eiji; Seki, Makoto; Fusamoto, Hideyuki; Kamada, Takenobu
AB An in vivo model of hepatitis C virus (**HCV**) infection is needed to enable investigation of the mechanism of the liver injury that it causes. In this study, we used asialoglycoprotein receptor mediated gene delivery to obtain expression of the complementary DNA (cDNA) coding the core and part of the **envelope 1** protein of **HCV** because selective delivery to the hepatocytes has been reported to be attained with this method. The optimum carrier-DNA ratio was examd. using in vitro transfection and found to be important for the efficiency of this method. In transfection in vivo, microautoradiog. examn. showed that the transfected plasmids were delivered selectively to the liver parenchymal cells. To obtain an immunohistochem. detectable level of protein expression in rodent liver, some modifications for increasing the in vivo transfection efficiency were performed; a lysosomal enzyme inhibitor, chloroquine, was used and the administration route of the carrier-DNA complex was changed from the tail vein to the portal vein. On the bases of these results, in vivo transfection with expression vector of **HCV** core/E1 region was performed. In rat liver transfected by intraportal injection with chloroquine, the transcript RNA and the core protein were detected. These results indicated that the **HCV** core/E1 expression vector was not merely delivered but also successfully expressed in the liver using asialoglycoprotein receptor mediated gene delivery. The no. of the **HCV** core expressing cells in the transfected liver was similar to that in patients with hepatitis C. These in vivo transfected animals should be useful for investigating the role of this region in the liver injury caused by **HCV**.

L2 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:556035 CAPLUS
DOCUMENT NUMBER: 122:310542

TITLE: Classification of hepatitis C virus into major types and subtypes based on molecular evolutionary analysis
AUTHOR(S): Ohba, Ken-ichi; Mizokami, Masashi; Ohno, Tomoyoshi; Suzuki, Kaoru; Orito, Etsuro; Ina, Yasuo; Lau, Johnson Y. N.; Gojobori, Takashi
CORPORATE SOURCE: Second Department of Internal Medicine, Nagoya City University Medical School, Kawasumi, Mizuho, Nagoya, 467, Japan
SOURCE: Virus Res. (1995), 36(2-3), 201-14
CODEN: VIREDF; ISSN: 0168-1702
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Classification of hepatitis C virus into major types and subtypes based on molecular evolutionary analysis
SO Virus Res. (1995), 36(2-3), 201-14
CODEN: VIREDF; ISSN: 0168-1702
AU Ohba, Ken-ichi; Mizokami, Masashi; Ohno, Tomoyoshi; Suzuki, Kaoru; Orito, Etsuro; Ina, Yasuo; Lau, Johnson Y. N.; Gojobori, Takashi
AB Mol. evolutionary anal. was applied to det. the no. of hepatitis C virus (**HCV**) types and subtypes based on all the **HCV** nucleotide sequences available from the DNA data banks (DDBJ, GenBank (NCBI), EMBL) and the literature. There was an excellent concordance among the types and subtypes assigned based on different **HCV** genomic regions. Only one **HCV** isolate was assigned to different **HCV** types based on the 5' non-coding (NC) and **envelope 1** (E1) regions. The 5' NC region was well conserved and could be used to assign only types and not subtypes. From the sequence data available there were 13 subtypes based on the core region and 14 subtypes based on the E1 and non-structural protein 5 (NS5) regions.

L2 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:209827 CAPLUS
DOCUMENT NUMBER: 122:156064
TITLE: Hepatitis C virus variants from Vietnam are classifiable into the seventh, eighth, and ninth major genetic groups
AUTHOR(S): Tokita, Hajime; Okamoto, Hiroaki; Tsuda, Fumio; Song, Pham; Nakata, Susumu; Chosa, Tohru; Iizuka, Hisao; Mishiro, Shunji; Miyakawa, Yuzo; Mayumi, Makoto
CORPORATE SOURCE: Immunol. Div., Jichi Med. Sch., Tochigi-Ken, Japan
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1994), 91(23), 11022-6
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Hepatitis C virus variants from Vietnam are classifiable into the seventh, eighth, and ninth major genetic groups
SO Proc. Natl. Acad. Sci. U. S. A. (1994), 91(23), 11022-6
CODEN: PNASA6; ISSN: 0027-8424
AU Tokita, Hajime; Okamoto, Hiroaki; Tsuda, Fumio; Song, Pham; Nakata, Susumu; Chosa, Tohru; Iizuka, Hisao; Mishiro, Shunji; Miyakawa, Yuzo; Mayumi, Makoto
AB Thirty-four (41%) of 83 hepatitis C virus (**HCV**) isolates from com. blood donors in Vietnam were not classifiable into genotype I/1a, II/1b, III/2a, IV/2b, or V/3a; for 15 of them, the sequence was detd. for

1.6 kb in the 5'-terminal region and 1.1 kb in the 3'-terminal region. Comparison of the 15 Vietnamese isolates among themselves and with reported full or partial **HCV** genomic sequences indicated that they were classifiable into 4 major groups (groups 6-9) divided into 6 genotypes (6a, 7a, 7b, 8a, 8b, and 9a). Vietnamese **HCV** isolates of genotypes 7a, 7b, 8a, 8b, and 9a were significantly different from those classified into groups 4, 5, and 6 based on divergence within partial sequences; those of genotype 6a were homologous to a Hong Kong isolate (HK2) of genotype 6a. Phylogenetic trees based on the **envelope 1** (E1) gene (576 bp) of 55 isolates and a part of the nonstructural 5 (NS5) region (1093 bp) of 43 isolates revealed .gtoreq.9 major groups, 3 of which (groups 7, 8, and 9) were identified only in Vietnamese blood donors. With a prospect that many more **HCV** isolates with significant sequence divergence will be reported from all over the world, the domain of the **HCV** genome to be compared and criteria for grouping/typing and genotyping/subtyping will have to be detd., so that they may be correlated with virol., epidemiol., and clin. characteristics.

L2 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:673420 CAPLUS
DOCUMENT NUMBER: 121:273420
TITLE: Sequence analysis of the core gene of 14 hepatitis C virus genotypes
AUTHOR(S): Bukh, Jens; Purcell, Robert H.; Miller, Roger H.
CORPORATE SOURCE: Lab. Infectious Dis., Natl. Inst. Allergy Infectious Dis., Bethesda, MD, 20892, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1994), 91(17), 8239-43
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Sequence analysis of the core gene of 14 hepatitis C virus genotypes
SO Proc. Natl. Acad. Sci. U. S. A. (1994), 91(17), 8239-43
CODEN: PNASA6; ISSN: 0027-8424
AU Bukh, Jens; Purcell, Robert H.; Miller, Roger H.
AB We previously sequenced the 5' noncoding region of 44 isolates of hepatitis C virus (**HCV**), as well as the **envelope 1** (E1) gene of 51 **HCV** isolates, and provided evidence for the existence of at least 6 major genetic groups consisting of at least 12 minor genotypes of **HCV** (i.e., genotypes I/1a, II/1b, III/2a, IV/2b, 2c, V/3a, 4a-4d, 5a, and 6a). We now report the complete nucleotide sequence of the putative core (C) gene of 52 **HCV** isolates that represent all of these 12 genotypes as well as two addnl. genotypes provisionally designated 4e and 4f that we identified in this study. The phylogenetic anal. of the C gene sequences was in agreement with that of the E1 gene sequences. A major division in the genetic distance was obsd. between **HCV** isolates of genotype 2 and those of the other genotypes in anal. of both the E1 and C genes. The C gene sequences of 9 genotypes have not been reported previously (i.e., genotypes 2c, 4a-4f, 5a, and 6a). Our anal. indicates that the C gene-based methods currently used to det. the **HCV** genotype, such as PCR with genotype-specific primers, should be revised in light of these data. We found that the predicted C gene was exactly 573 nt long in all 52 **HCV** isolates, with an N-terminal start codon and no in-frame stop codons. The nucleotide and predicted amino acid identities of the C gene sequences were in the range of 79.4-99.0% and 85.3-100%, resp. Furthermore, we mapped universally conserved, as well as genotype-specific, nucleotide and deduced amino acid sequences of the C

gene. The predicted C proteins of the different **HCV** genotypes shared the following features: (1) high content of proline residues, (2) high content of arginine and lysine residues located primarily in three domains with 10 such residues invariant at positions 39-62, (3) a cluster of 5 conserved tryptophan residues, (4) two nuclear localization signals and a DNA-binding motif, (5) a potential phosphorylation site with a serine-proline motif, and (6) three conserved hydrophilic domains that have been shown by others to contain immunogenic epitopes. Thus, we have extended anal. of the predicted C protein of **HCV** to all of the recognized genotypes, confirmed the existence of highly conserved regions of this important structural protein, and demonstrated that the genetic relatedness of **HCV** isolates is equiv. when analyzing the most conserved (i.e., C) and the most variable (i.e., EI) genes of the **HCV** genome.

L2 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:126371 CAPLUS
DOCUMENT NUMBER: 120:126371
TITLE: At least 12 genotypes of hepatitis C virus predicted by sequence analysis of the putative E1 gene of isolates collected worldwide
AUTHOR(S): Bukh, Jens; Purcell, Robert H.; Miller, Roger H.
CORPORATE SOURCE: Lab. Infect. Dis., Natl. Inst. Allergy Infect. Dis., Bethesda, MD, 20892, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1993), 90(17), 8234-8
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
TI At least 12 genotypes of hepatitis C virus predicted by sequence analysis of the putative E1 gene of isolates collected worldwide
SO Proc. Natl. Acad. Sci. U. S. A. (1993), 90(17), 8234-8
CODEN: PNASA6; ISSN: 0027-8424
AU Bukh, Jens; Purcell, Robert H.; Miller, Roger H.
AB In a previous study the authors sequenced the 5' noncoding (NC) region of 44 isolates of hepatitis C virus (**HCV**) and identified heterogeneous domains that provided evidence for addnl. genetic groups of **HCV** not previously recognized. In this study the authors have detd. the complete nucleotide sequence of the putative **envelope 1** (E1) gene in 51 **HCV** isolates from around the world and found that they could be grouped into at least 12 distinct genotypes. The E1 gene sequence of 8 of these genotypes has not been reported previously. Although the genetic relatedness of **HCV** isolates detd. by the previous anal. of the 5' NC region predicted the relationships obsd. in the E1 gene, anal. of the 5' NC sequence alone did not accurately predict all **HCV** genotypes. The nucleotide and amino acid sequence identities of the E1 gene among **HCV** isolates of the same genotype were in the range of 88.0-99.1% and 89.1-98.4%, resp., whereas those of **HCV** isolates of different genotypes were in the range of 53.5-78.6% and 49.0-82.8%, resp. The latter differences are similar to those found when comparing the **envelope** gene sequences of the various serotypes of the related flaviviruses as well as other RNA viruses. The authors found that some genotypes of **HCV** were widely distributed around the world, whereas others were identified only in discrete geog. regions. Four genotypes were identified exclusively in Africa and comprised the majority of **HCV** isolates on that continent. The E1 gene was exactly 576 nucleotides in length in all 51

HCV isolates with no in-frame stop codons. Anal. of the predicted E1 protein identified several conserved domains that may be important for maintaining its biol. function: (1) eight invariant cysteine residues, (2) three potential N-linked glycosylation sites, (3) a domain of nine amino acids (GHRMAWDMM), and (4) an amino acid doublet (GV) near the putative cleavage site at the C terminus of the protein. In conclusion, the discovery of at least 12 genotypes of **HCV** has important implications for **HCV** diagnosis and vaccine development.

L2 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:667866 CAPLUS
DOCUMENT NUMBER: 119:267866
TITLE: Suppression of hepatitis B virus expression and replication by hepatitis C virus core protein in HuH-7 cells
AUTHOR(S): Shih, Chwen Ming; Lo, Szecheng J.; Miyamura, Tatsuo; Chen, Shiow Yi; Lee, Yan Hwa Wu
CORPORATE SOURCE: Inst. Biochem., Natl. Yang-Ming Med. Coll., Taipei, 112, Taiwan
SOURCE: J. Virol. (1993), 67(10), 5823-32
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Suppression of hepatitis B virus expression and replication by hepatitis C virus core protein in HuH-7 cells
SO J. Virol. (1993), 67(10), 5823-32
CODEN: JOVIAM; ISSN: 0022-538X
AU Shih, Chwen Ming; Lo, Szecheng J.; Miyamura, Tatsuo; Chen, Shiow Yi; Lee, Yan Hwa Wu
AB Hepatitis B and C viruses (HBV and **HCV**, resp.) are assocd. with acute and chronic liver diseases and hepatocellular carcinoma. To elucidate the mol. status of superinfection with these two hepatitis viruses, the authors cotransfected the full-length or truncated version of **HCV** structural genes (core and **envelope 1**) together with the cloned HBV DNA into a human hepatoma cell line (HuH-7). Expression of HBV-specific major transcripts (3.5 and 2.1 kb), as well as HBV antigens (hepatitis B surface antigen and hepatitis B e and core antigens), was reduced about two- to fourfold by the presence of the **HCV** structural genes. In addn., the secretion of HBV viral particles, including the viral nucleocapsid and mature virion, was drastically suppressed about 20-fold. Anal. of the intracellular HBV core protein-assocd. nucleic acid indicated that the encapsidated HBV pregenomic RNA was similarly reduced about 14-fold. Deletion anal. of the **HCV** structural genes demonstrated that the core gene alone or the fragment contg. the core protein's N-terminal 122 amino acid residues conferred the same level of suppressive activity as the full-length structural genes. By indirect immunofluorescence, the authors found that the core protein of **HCV** was located in the cytoplasm of transfected HuH-7 cells at day 3 posttransfection and was targeted to the nucleus at day 6. Thus, the kinetics of the suppressive effect exerted by **HCV** constructs matched the timing of core protein entrance into the nucleus. The authors' results substantiate the clin. finding that HBV

markers are suppressed by superinfection with **HCV** and further imply that this inhibitory effect may occur in the processes of transcription and encapsidation of HBV pregenomic RNA and may be mediated by the core protein of **HCV**. The deduced amino acid sequence of the **HCV** core protein has revealed that it is a basic protein which contains a putative DNA-binding motif (SPRG), as well as triplicate nuclear localization signals and several putative protein kinase A and C recognition sites. These characteristics imply that the **HCV** core protein can also function as a gene-regulatory protein.

L2 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:601360 CAPLUS
DOCUMENT NUMBER: 119:201360
TITLE: Antigenic regions within the hepatitis C virus **envelope 1** and non-structural proteins: Identification of an IgG3-restricted recognition site within the **envelope 1** protein
AUTHOR(S): Sallberg, M.; Ruden, U.; Wahren, B.; Magnius, L. O.
CORPORATE SOURCE: Dep. Virol., Karolinska Inst., Stockholm, Swed.
SOURCE: Clin. Exp. Immunol. (1993), 91(3), 489-94
CODEN: CEXIAL; ISSN: 0009-9104
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Antigenic regions within the hepatitis C virus **envelope 1** and non-structural proteins: Identification of an IgG3-restricted recognition site within the **envelope 1** protein
SO Clin. Exp. Immunol. (1993), 91(3), 489-94
CODEN: CEXIAL; ISSN: 0009-9104
AU Sallberg, M.; Ruden, U.; Wahren, B.; Magnius, L. O.
AB Antibody binding to antigenic regions of hepatitis C virus (**HCV**) **envelope 1** (E1; residues 183-380), E2/non-structural (NS) 1 (residues 380-437), NS1 (residues 643-690), and NS4 (1684-1751) proteins were assayed with 50 sera for antibodies to **HCV** (anti-**HCV**) and with 46 sera without anti-**HCV**. Thirty-four peptides, 18 residues long with an eight-amino acid overlap within each **HCV** region, were synthesized and tested with all 96 sera. Within the E region 183-380, the major binding site was located to residues 203-220, and was recognized by eight sera. Within the E2/NS1 region 380-437, the peptide covering residues 410-427 was recognized by two sera, and within the NS1 region 643-690, peptides covering residues 663-690 were recognized by four sera. Within the NS4 region 1684-1751, 27 sera were reactive to one or more of the NS4 peptides, and 21 out of these were reactive with peptide 1694-1711. One part of the major binding site could be located to residues 1701-1704, with the sequence Leu-Tyr-Arg-Glu. The IgG1, IgG3 and IgG4 subclasses were reactive with the five antigenic regions of **HCV** core, residues 1-18, 11-28, 21-38, 51-68 and 101-118. Reactivity to the major **envelope** site consisted almost exclusively of IgG3, and reactivity to the major site of NS4 consisted only of IgG1. Thus, a non-restricted IgG response to linear **HCV** -encoded binding sites was found to the core protein, whereas IgG subclass-restricted linear binding sites were found within the E1 protein, and within the NS4 protein.

L2 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:510547 CAPLUS
DOCUMENT NUMBER: 119:110547
TITLE: Hepatitis C virus (**HCV**) genomic sequences for diagnostics and therapeutics
INVENTOR(S): Cha, Taian; Beall, Eileen; Irvine, Bruce; Kolberg, Janice; Urdea, Michael S.
PATENT ASSIGNEE(S): Chiron Corp., USA
SOURCE: PCT Int. Appl., 186 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9219743	A2	19921112	WO 1992-US4036	19920508
WO 9219743	A3	19931125		
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
AU 9221558	A1	19921221	AU 1992-21558	19920508
AU 668355	B2	19960502		
EP 585398	A1	19940309	EP 1992-913881	19920508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06508026	T2	19940914	JP 1992-512055	19920508
HU 69609	A2	19950928	HU 1993-3166	19920508
PL 169880	B1	19960930	PL 1992-301282	19920508
PL 170151	B1	19961031	PL 1992-312096	19920508
RU 2155228	C2	20000827	RU 1993-58449	19920508
CZ 288720	B6	20010815	CZ 1993-2377	19920508
CZ 288722	B6	20010815	CZ 1996-1210	19920508
RO 117267	B1	20011228	RO 1993-1493	19920508
NO 9304019	A	19931105	NO 1993-4019	19931105
US 6190864	B1	20010220	US 1994-221653	19940401
US 6071693	A	20000606	US 1995-441971	19950516
US 6214583	B1	20010410	US 1995-442144	19950516
US 6297370	B1	20011002	US 1995-441970	19950516

PRIORITY APPLN. INFO.:

US 1991-697326	A	19910508
CS 1993-2377	A3	19920508
US 1992-881528	B1	19920508
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TI Hepatitis C virus (**HCV**) genomic sequences for diagnostics and therapeutics
SO PCT Int. Appl., 186 pp.
CODEN: PIXXD2
IN Cha, Taian; Beall, Eileen; Irvine, Bruce; Kolberg, Janice; Urdea, Michael S.
AB The cDNA probe sequences for the NS5, **envelope 1**, 5'UT, and the core regions of 5 genotypes of **HCV** are given. These cDNA probes can be used for detection of **HCV** by e.g. sandwich hybridization. Also they can be used for prepg. antigenic peptides for induction of antibodies to **HCV** for the title purposes.

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